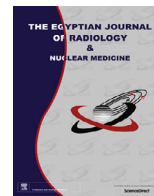




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Original Article

Value of MR enterography in assessment of Crohn's disease: Correlation with capsule endoscopy and colonoscopy

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ABSTRACT

Objectives: To assess the accuracy of Magnetic Resonance Enterography (MRE) in determining site, extent and complications of Crohn's disease, in correlation with capsule endoscopic and colonoscopy findings. **Patients and methods:** We performed an observational prospective study for 30 patients with suspected Crohn's disease or already diagnosed patients with Crohn's disease (CD). Bowel inflammatory changes were analyzed for each involved bowel segment. Associated lymph nodes, abscesses, and fistulas were also evaluated.

Results: MRE was diagnostic for small bowel inflammatory changes with sensitivity and specificity values of 76% and 90% respectively as compared to 80% and 88% for capsule endoscopy, with an overall accuracy of 83% as compared to capsule endoscopy.

For large bowel inflammatory changes, MRE showed sensitivity and specificity values of 82% and 80% respectively as compared to 84% and 85% for colonoscopy, with an overall accuracy of 81% as compared to colonoscopy.

All severely inflamed segments were correctly identified, and there were no false positive findings in this study.

Conclusion: MRE is practicable, non-invasive and provides additional information regarding areas not accessible with endoscopy.

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1. Introduction

Crohn's disease and ulcerative colitis are the most frequent specific inflammatory bowel diseases (IBD) with a prevalence of approximately one in 500, and has increased in the past 50 years [1]. There are two peaks for Crohn's disease: one in adolescents and young adults between 15 and 25 years old and a second shallow peak seen in the 50–80 year old age group [2].

CD is an incurable chronic disease that can affect the entire gastrointestinal system. Histologically, it affects the whole bowel wall, in contrast to ulcerative colitis, which affects the intestinal mucosal layer only. Because of these characteristic spreading features,

a group of patients develop major complications during the course of the disease, such as fistulas and abscesses [3].

The gold standard modality for diagnosis is upper and lower endoscopy along with conventional imaging [4]. Another new modality being used is capsule endoscopy which shows promising results and is well accepted by a significant group of patients [5].

Another important modality is Computed tomography (CT), yet CD is a lifelong condition with recurrent chronic relapsing course, making CT a less than ideal diagnostic tool for follow-up due to concerns over the hazards of cumulative radiation exposure [6].

On the other hand, MRE provides in one single study a detailed multiplanar, multiparametric, and multiphasic contrast-enhanced examination with high spatial resolution and very high tissue contrast allowing precise evaluation of intra-abdominal pathology, without the risk of radiation exposure [7].

MRE provides the benefit of full evaluation of mural and extramural manifestations of CD with the capability to differentiate between active inflammatory and chronic disease, allowing

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gastroenterologists and surgeons to plan the most ideal approach for best patient outcome [7].

The aim of this study was to evaluate the role of MRE in assessing suspected or already diagnosed cases of CD in comparison with endoscopy and colonoscopy.

2. Patients and methods

A preprocedural consent was taken as regards the volume of contrast agent to be given, and patient was informed with the procedure explaining the mild side effects they may encounter, if any.

Exclusion criteria included claustrophobic patients and contraindications to MRI (as metallic implants, pacemaker...).

2.1. Patients

From August 2014 to September 2015, we prospectively evaluated 30 consecutive patients with MRE (16 females, 14 males, age range 11–48 years old, median age around 29.7). For all patients, a small bowel capsule endoscopy and ileocolonoscopy followed the MRE study within a few days to maximum 4 weeks later.

Twenty-one patients had known Crohn's disease and nine were clinically disease suspected but with no definitive prior diagnosis. Symptoms ranged from chronic diarrhea to acute abdominal pain.

6 patients went for surgery; 2 patients were with deep intra-abdominal abscesses, 2 patients were for an anterior abdominal wall fistula and two other patients were with suspected enterovesical fistulas.

2.2. MRE technique

Appropriate patient preparation is the first most important step for a good quality MRE study. Patients were instructed to take nothing by mouth for 4–6 h prior to the study.

Adequate small bowel distention was achieved by gradual oral administration of Mannitol 20%. Mannitol is a hyperosmolar agent not absorbed across the intestinal mucosa ensuring good luminal distention.

Amount of oral contrast agent depends on the patient's age and size with an average adult drinking an amount of 250 ml Mannitol in 750 ml saline.

The patient was told to arrive around 90 min before their MRI appointment and to drink the oral contrast agent gradually throughout one hour for adequate distention and separation of the small bowel loops- one cup every 15 min.

Around 1 mg intravenous Buscopan (butylscopolamine) was given just before the procedure to reduce bowel spasm and motility.

MRE was done on a 3T (General Electric- USA) in a supine position. We began the study with a coronal T2 SSFSE (Repetition time (ms) (TR):1693, Echo time (ms) (TE): 180, Section thickness (mm) (ST):7, Gap (mm): 8, Field of View (mm) (FOV): 420 × 420) and a coronal heavy T2 (TR: 6375, TE: 595.4, ST: 20, Gap: 10, FOV: 420 × 420) followed by axial sequences.

Two axial sequences were taken: one axial heavy T2 (TR: 4250, TE: 587.3, ST: 10, Gap: 10, FOV: 40 × 420) and an axial FIESTA sequence (TR: 4.4, TE: 1.5, ST:6, Gap: 7, FOV: 400 × 400).

A dynamic cine sequence was also taken before the administration of contrast. Cine motility imaging was performed in a coronal plane with a steady state free-precession type sequence without fat saturation (FIESTA) (TR: 4.3, TE: 1.5, ST: 7, Gap: 8, FOV: 420 × 420).

Fat-suppressed 3D LAVA FLEX sequences were then taken. Fat suppression was essential for proper evaluation of inflammatory and surrounding mesenteric soft tissue changes. Precontrast and multiphase dynamic postcontrast images were obtained in both axial and coronal planes (TR: 6.6, TE: 1.8, ST: 4.8, Gap: 2.4, FOV: 440 × 440).

Optimal timing of postcontrast images after injection of contrast was crucial. Maximum enteric enhancement occurs approximately 50 s after the start of contrast injection and thus should coincide with the midpoint of the first postcontrast sequence. Thus, a 22-s long 3D LAVA FLEX sequence should be started around 40 s after the start of injection. Our facility used a standard weight-based dose of the high relaxivity contrast agent MultiHance (gadobenate dimeglumine), which was injected at 2 ml/s, followed by a 40-ml saline flush at the same rate.

Dynamic progression of enhancement throughout the course of the study provided important diagnostic information. We started with a coronal 3D LAVA FLEX sequence 40 s after the start of contrast administration (center of k-space of this sequence is at around 50 s). After allowing the patient to take several rapid breaths, we immediately followed with an axial data set of the same area of coverage. We then repeated coronal and axial data sets and finished the study with a third coronal LAVA FLEX. Although it seems as a long sequence at first glance, all of these were taken within 3–4 min. The acquisition of multiple sequential postcontrast data sets allowed for evaluation of progression of enhancement in the affected bowel segments.

Extra Diffusion-Weighted Images (DWI) axial sequences were taken in all cases using b values at 0, 400 and 800.

2.3. Image analysis

For bowel evaluation, we divided the small bowel into four sub-segments (duodenum, jejunum, ileum and terminal ileum). The colon was divided into four segments as well (ascending, transverse, descending and rectosigmoid).

A bowel segment was considered as diagnostic when properly distended and clearly visualized without the presence of any major motion artifacts.

Bowel loops were evaluated as regards thickness, degree and pattern of enhancement, the presence of surrounding inflammatory changes with careful assessment of mesenteric LNs, adjacent mesenteric fat changes and extra-intestinal findings. Findings were classified as acute, chronic or acute on top of chronic disease (Table 1) [8].

Cine motility sequence was of superadded value as both acutely inflamed and fibrotic bowel segments demonstrated alterations in normal bowel peristalsis. Acutely inflamed segments showed hypokinetic movement, while fibrostenotic segments showed

Table 1
Acute and chronic features of CD by MRE.

MRE	Active disease	Chronic disease
Mural thickness and enhancement	Moderate/strong	Mild to moderate-less than acute
Mural edema	Yes	Mild
Engorged vasa recta	Yes	No
Hyperenhancing mesenteric lymph nodes	Yes	No
Fibrofatty proliferation	May be seen	Frequently seen
Enteric/perianal fistula	Yes	Yes

Table 2

Parameters assessed on MRE and number of patients affected.

Parameters assessed	No. of patients/30
• Is there duodenal or jejunal affection?	13
• Is there extensive small bowel disease?	4
• Is the disease only involving the terminal ileum and ileocecal region?	14
• Any small bowel strictures?	8
• Is there large bowel/colonic affection?	7
<i>Extraintestinal/mesenteric complications</i>	
• Enterointeric fistula	2
• Enterocolic fistula	1
• Enterovaginal fistula	0
• Enterovesical fistula	2
• Enterocutaneous fistula	2
• Perianal fistula	3
• Intra-abdominal abscess	2
• Deep gluteal abscess	1

areas of narrowing with proximal dilatation and consequent to-and-fro movement in the proximal segments [9].

Data were tabled and statistically analyzed using SPSS vs. 15. Nonparametric data were expressed as number and percentage. Sensitivity, specificity, positive and negative predictive values were expressed as percentages for ease of interpretation.

3. Results

Several parameters were assessed in the MRE study to aid in the diagnosis and disease staging (Table 2).

Sensitive indicators of CD were wall thickening and wall enhancement reaching 78% and 82% respectively. Specific signs

Table 3

Results of both MRE and endoscopy.

Bowel segment affection	No. of patients/30	
	MRE	Endoscopy
<i>Small bowel</i>		
Duodenum	7	9
Jejunum	9	13
Ileum	13	14
Terminal ileum/ileocecal junction	20	21
<i>Colon</i>		
Ascending colon	1	2
Transverse colon	1	1
Descending colon	2	2
Rectosigmoid	3	4

and indicators were Coomb's signs, enhancing adenopathy and extra-intestinal findings reaching around 92%, 89% and 100% respectively.

Most patients showed involvement of the small bowel, with the terminal ileum and ileocecal junction the most commonly involved segment (Fig. 1). MRI sensitivity of detection of ileal and terminal ileum disease reached around 92% and 95% respectively.

Small and large bowel segments were properly evaluated and compared to endoscopy and colonoscopy results (Table 3). MRE identified 64/84 segments involved. MRE showed identical results to endoscopy and colonoscopy in 56/84 segments, and underestimated results were seen in 5 of the cases and a more severe picture in 4 cases. Missed cases were mainly in the duodenum and jejunum segments.

Findings were further on classified into acute (Fig. 2), chronic (Fig. 3) or chronic with acute exacerbation on top (Fig. 4), according to imaging findings.

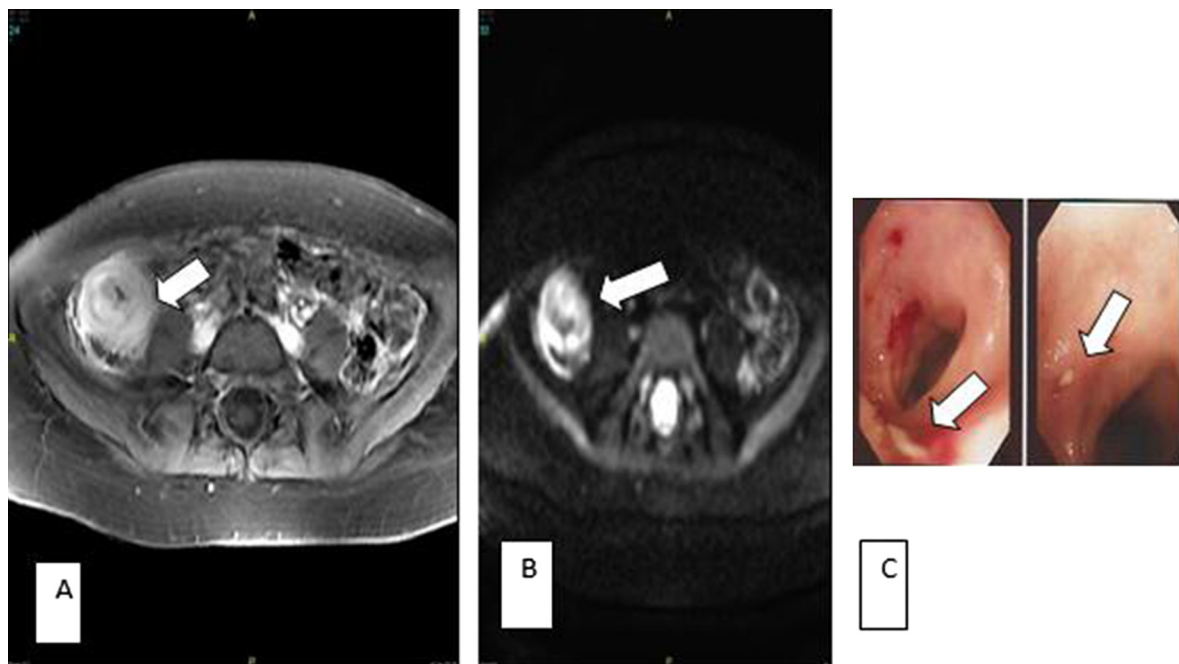


Fig. 1. 15 year old presented for the first time with acute abdominal pain. (A) Axial postcontrast 3D LAVA FLEX showing marked transmural wall thickening and enhancement in the terminal ileum. (B) DW1 showing restricted diffusion denoting acute inflammatory changes. Findings were confirmed on endoscopy. (C) Colonoscopy images showing multiple ulcers and erosions in the terminal ileum with acute inflammatory changes.

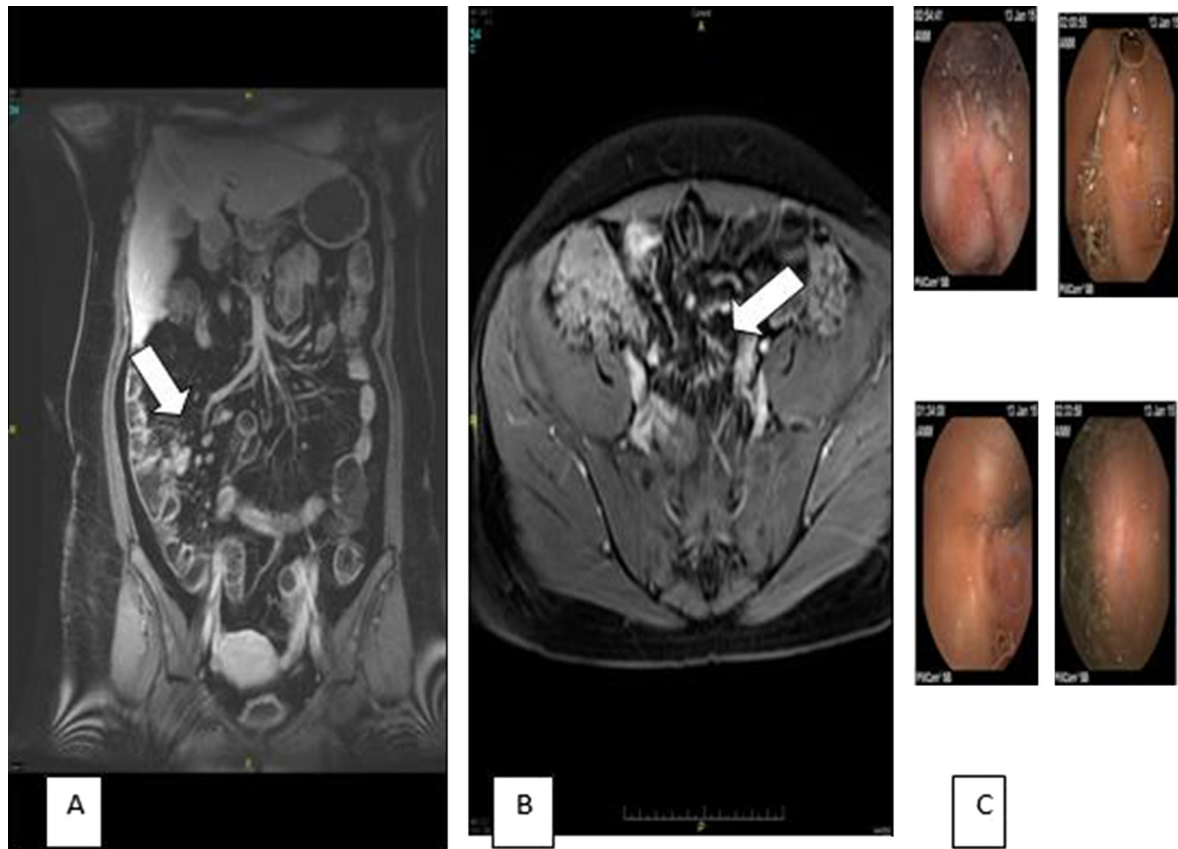


Fig. 2. Two young patients with acute changes of CD. (A) Coronal postcontrast 3D LAVA FLEX image showing multiple hyper enhancing mesenteric lymph nodes in right iliac fossa. (B) Axial postcontrast 3D LAVA FLEX image demonstrating the typical appearance of the Coomb sign (arrow) with wall enhancement of the adjacent small bowel loops. (C) Capsule endoscopy images of the patient showing aphthous ulcers with edematous mucosa.



Fig. 3. 43 year old male patient with known CD complaining of daily abdominal cramping with eating. (A) Coronal SSFSE image showing fibrotic thickening and stricture of a segment of the distal ileum. (B) Coronal postcontrast 3D LAVA FLEX image showing moderate enhancement of the walls.

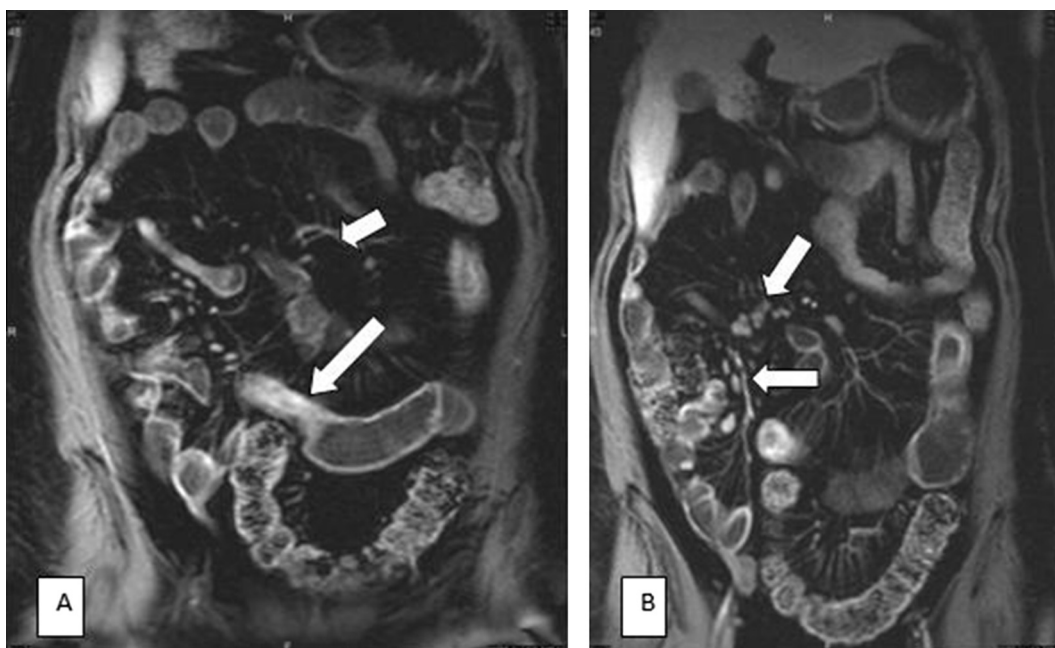


Fig. 4. 37 year old patient with known CD presented with acute right lower quadrant pain. (A) Coronal postcontrast image shows inflammatory fibrotic stricture of an ileal bowel loop (long arrow) with significant fibrofatty proliferation (short arrows). (B) Coronal postcontrast image shows acute inflammatory changes on top with multiple enhancing lymph nodes and congested mesentery (Coomb's sign).



Fig. 5. 18 years old patient with known CD. Axial postcontrast image showing a right intersphincteric fistula showing enhancing walls (arrow).

From the 21 patients with known CD, 9 cases showed acute changes on top of chronic changes in the MRE study while 12 patients showed only chronic changes.

From the 9 patients suspected to have CD, 8 patients showed acute inflammatory changes by endoscopy with one case missed by MRE.

Overall, our study demonstrated a sensitivity of 76% and a specificity of 90% with positive predictive value (PPV) and negative

predictive value (NPV) of 85% and 70% respectively in comparison with capsule endoscopy. In comparison with colonoscopy, MRE demonstrated a sensitivity of 82% and a specificity of 80% with PPV and NPV of 83% and 80% respectively. Overall accuracy of MRE compared to capsule endoscopy and colonoscopy was 83% and 81% respectively.

3.1. Evaluation of extra intestinal findings/complications

Perianal fistulae were seen in 3/30 patients: 2 intersphincteric and 1 transsphincteric perianal fistula (Fig. 5). High-resolution contrast-enhanced sequences showed typical enhancement in the collapsed walls of the tract. One perianal fistula was missed by MRE as was suspected clinically.

Enterocutaneous fistula was detected in 2 patients appearing as a long thin enhancing tract extending from the ileum to the anterior abdominal wall (Fig. 6).

Enteroenteric fistulae were seen in two different patients where multiple adjacent bowel loops were adherent to each other giving the characteristic stellate appearance on SSFSE and contrast-enhanced sequences (Fig. 7).

Two patients showed suspicious enterovesical fistulas with an enhancing tract seen related to the bladder dome, with one of them showing tenting of the dome (Fig. 8). Findings were confirmed on surgery.

One patient showed a suspected enterocolic fistula with a short enhancing tract seen connecting the sigmoid colon to a distal ileal loop (Fig. 9).

Two intra-abdominal abscesses were diagnosed in two separate patients, showing the classic T2 hyperintense fluid collection with an enhancing rim postcontrast. DWI sequences were of additive value and displayed restricted diffusion, confirming our conventional sequence findings (Fig. 10).

One patient showed a small right gluteal abscess showing post-contrast wall enhancement (Fig. 11).

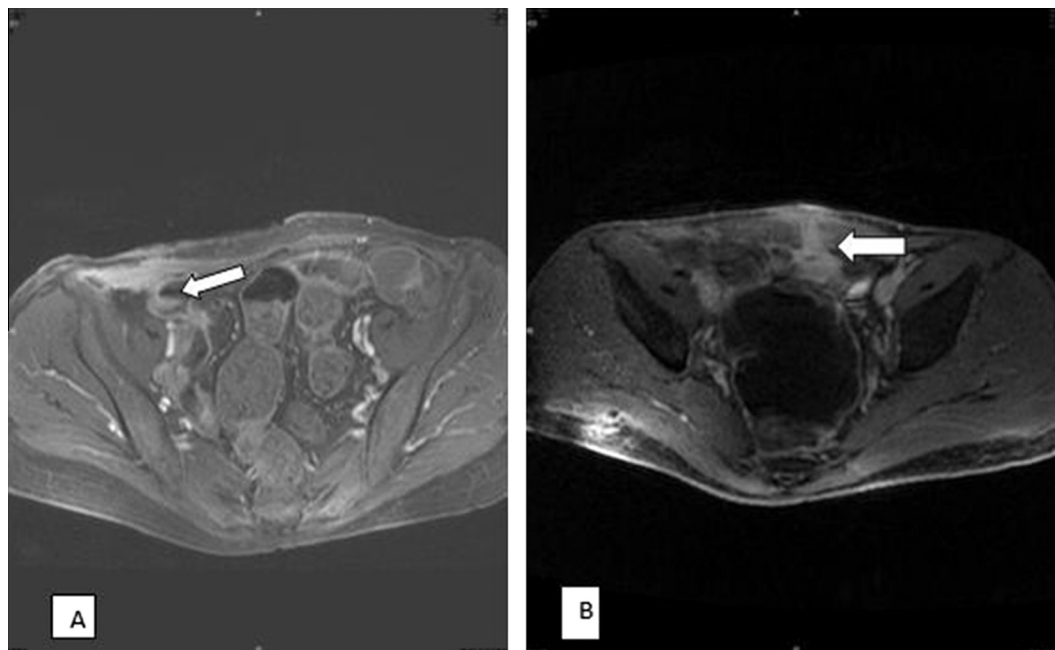


Fig. 6. Enterocutaneous fistula in two different patients with known CD. (A and B) Axial postcontrast images displaying a hyperintense thick enhancing tract from the ileum to the skin (arrows).

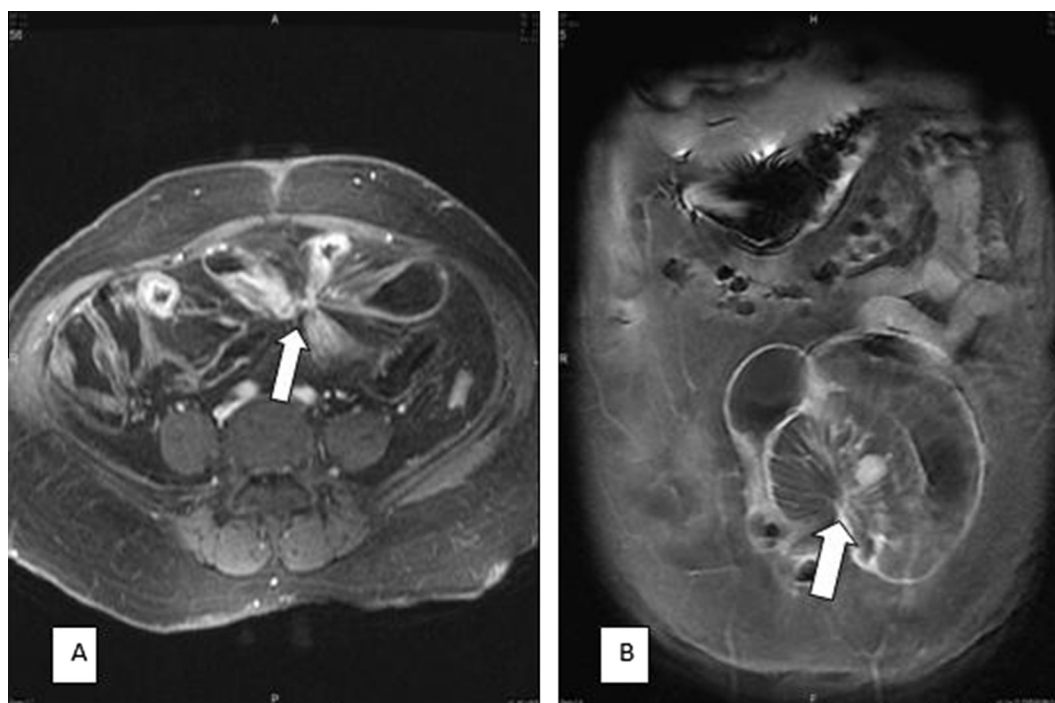


Fig. 7. Enteroenteric fistula in a 40 years old patient known CD presented with diarrhea. (A) Axial and (B) Coronal postcontrast images showing the multiple connecting loops of the proximal ileum giving the classic “stellate appearance”. Note the enhancing lymph nodes and Coomb’s sign denoting active inflammation on top.

Table 4 shows sensitivity, specificity and accuracy of MRE compared to endoscopy. MRE showed a sensitivity of 76%, specificity of 90% and an accuracy of 83% compared to capsule endoscopy which showed a sensitivity of 80% and a specificity of 88%.

Table 5 shows sensitivity, specificity and accuracy of MRE compared to colonoscopy. MRE showed a sensitivity of 82%, specificity of 80% and an accuracy of 81% compared to colonoscopy which showed a sensitivity of 85% and a specificity of 85%.



Fig. 8. Enterovesical fistula in two different patients. (A) Coronal postcontrast image demonstrating an enhancing tract between the bowel and the bladder dome (arrow). (B) Coronal SSFSE image showing a suspicious fistula with tenting of the bladder dome (arrow). Findings were confirmed on surgery.

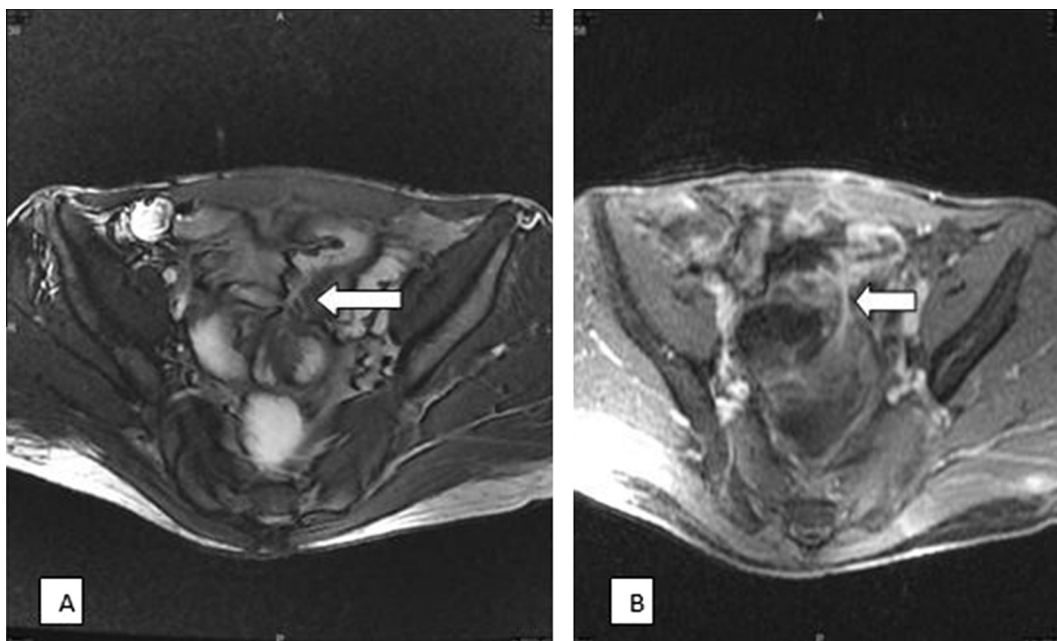


Fig. 9. Enterocolic fistula in a 33 year old patient with known CD. (A) Axial SSFSE image showing a small tract between the sigmoid colon and adjacent ileal loop with marked fibrosis (arrow). (B) Axial postcontrast image showing mild wall enhancement with no signs of active inflammation (arrow).

4. Discussion

CD is a chronic inflammatory bowel disorder, predominantly affecting young adults and requiring lifelong treatment and follow-up [10]. A number of possible factors have been suggested such as diet, autoimmune abnormalities, stress, infection, genetic factors, and smoking [11].

CD can affect any segment of the GI tract from the mouth down to the anal segment, with skip segments of bowel involvement being a specific characteristic feature of CD. Histologically, it is characterized by inflammation and the presence of non-caseating granulomas. Variable intramural involvement is seen that may extend through the full thickness of the bowel wall (transmural) to further involve the surrounding mesentery and soft tissues [7].

Table 4

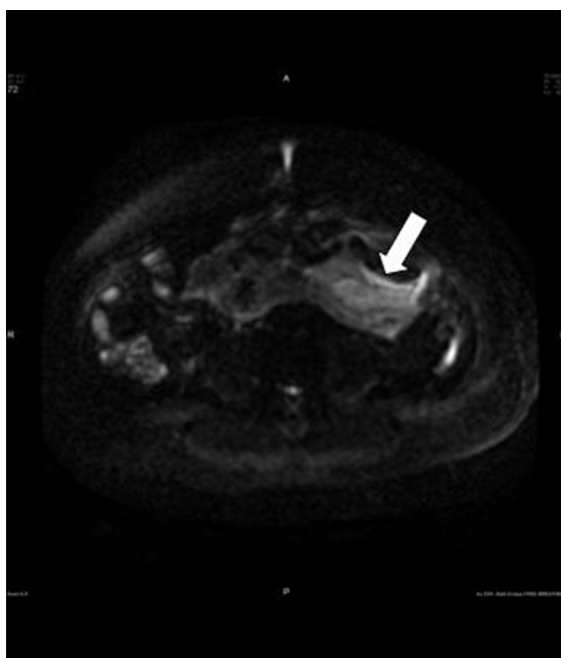
Sensitivity, specificity and accuracy of MRE compared to capsule endoscopy.

	Sensitivity	Specificity	Accuracy
MRE	76	90	83
Capsule endoscopy	80	88	90

Table 5

Sensitivity, specificity and accuracy of MRE compared to colonoscopy.

	Sensitivity	Specificity	Accuracy
MRE	82	80	81
Colonoscopy	85	85	92

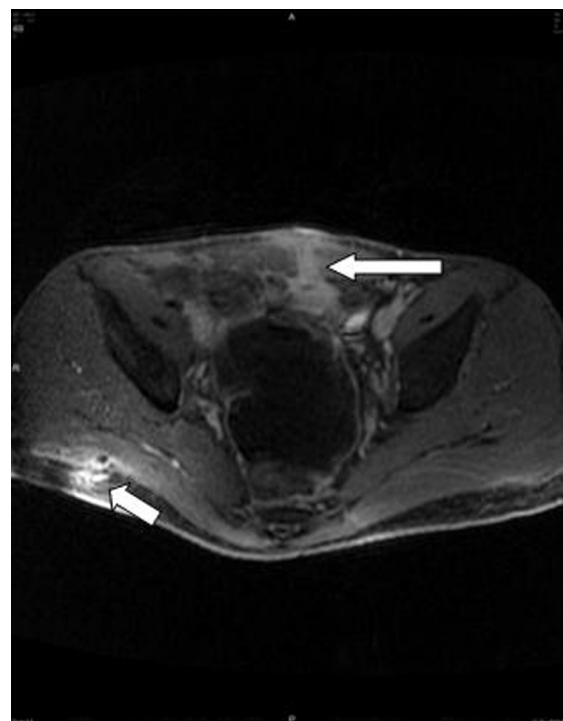
**Fig. 10.** Intra-abdominal abscess in a 29 patient known CD presented with fever and acute abdominal pain. DWI showed intra-abdominal inflammatory mass displaying restricted diffusion (arrow). Finding was confirmed in surgery.

Transmural involvement consequently results in strictures, fistulae and abscesses in up to 20% of patients [12].

Another important feature of CD is fibrofatty proliferation where there is increased deposition of fat along the mesenteric border of the bowel, which is clearly depicted by imaging and is a helpful diagnostic finding [13]. Extension of the inflammatory process outside the bowel wall was found to be associated with increased blood levels of C-reactive protein (CRP) [14].

Upper endoscopy followed by ileocolonoscopy is the method most commonly used by gastroenterologists to diagnose and evaluate inflammatory bowel disease, allowing direct visualization of the bowel lumen and mucosa. Its major advantage over all other modalities is that it allows simultaneous biopsy of abnormal segments, providing a definitive diagnosis [15]. Its disadvantage, however, is inability to evaluate extraintestinal findings or penetrating disease [16], its invasiveness, procedure-related discomfort and risk of perforation [17].

Capsule endoscopy in a short period of time has gained a well-established role in investigation of patients with Crohn's disease. It is a well-tolerated procedure and better accepted by patients compared with the routine endoscopy done. It has the advantage of being capable of detecting tiny ulcers and subtle mucosal

**Fig. 11.** Patient known CD with enterocutaneous fistula (long arrow) shows an associated small right gluteal abscess (small arrow). Axial Postcontrast Image shows a small rim-enhancing abscess in right gluteal region (arrow).

abnormalities and being able to assess the distal small bowel segments as well.

As for MRE, it allows dynamic acquisition of imaging data in multiple planes, which can categorize various stages in the disease process, whether acute inflammatory, chronic fibrotic changes or both [18]. It provides the benefit of a complete evaluation of mural and extra intestinal manifestations of CD in a single study. Furthermore, since CD patients are often young and have a lifelong chronic disease, repeated imaging for follow-up and disease monitoring can be done with no worries of radiation exposure [19].

Overall, our study demonstrated a sensitivity of 76% and a specificity of 90% with positive predictive value (PPV) and negative predictive value (NPV) of 85% and 70% respectively in comparison with capsule endoscopy which showed a sensitivity of 80% and a specificity of 88% with a PPV and NPV of 100% and 95% respectively.

On the other hand, MRE demonstrated a sensitivity of 82% and a specificity of 80% with PPV and NPV of 83% and 80% respectively compared to colonoscopy which showed a sensitivity of 84% and a specificity of 85% with a PPV and NPV of 90% and 98% respectively.

Overall accuracy of MRE compared to capsule endoscopy and colonoscopy was 83% and 81% respectively.

MRE was able to detect subtle mucosal findings and abnormal enhancement because of the differences in signal intensity between the luminal contents and the bowel wall. In our study, MRE showed good comparable results to both endoscopic techniques, as shown by Casciani et al. [20], Tillack et al. [21] and Albert et al. [22].

In our study compared to capsule endoscopy (CE), MRE missed 8 affected segments, and underestimated 5 of the cases and one acute CD case was missed. Around 78% of cases involving the duodenum and up to 69% of cases involving the jejunum were diagnosed.

Capsule endoscopy was slightly more sensitive and able to detect a greater number of segments affected and a greater number of lesions in the proximal small bowel segments. A study done by Gonzalez et al. showed that CE is slightly superior to MRE in detection of proximal small bowel lesions [23].

Suboptimal proximal small bowel depiction of inflammatory changes in our study was due to the reduced patient compliance for the constant ingestion of the required amount of fluid, hindering proper assessment of the proximal bowel.

With properly well-distended bowel loops, wall thickness and wall enhancement showed sensitivities of 78% and 82% respectively. Sinha et al. showed similar results with a sensitivity and specificity of 83–91% and 86–100% respectively [24].

Specific indicators were Coomb's sign, mesenteric adenopathy and extra-intestinal complications with values of 92%, 89% and 100% respectively. Grand et al. showed specificities of 91% and 93% for mesenteric vascular prominence and adenopathy respectively [25].

MRE in our study showed high sensitivity in the detection of inflammatory changes of the ileum and particularly the terminal ileum with sensitivities reaching 92% and 95% respectively. Our results were close to Yuksel et al. [26] which showed a sensitivity of 92% for assessment of ileal Crohn's disease.

An extra DWI axial sequence was taken in all cases using b values at 0, 400 and 800 and was of great help in documenting acute inflammatory changes. Two cases with suspected intra-abdominal abscesses were also made more evident by DWI.

CD complications, including transmural ulceration progressing to fistulae formation can be clearly demonstrated by MR, with sensitivity between 83% and 84% and specificity of 100% according to Rieber et al. [27].

The distinction between acute and chronic changes is crucial for guiding clinical management, particularly in patients with symptoms of acute exacerbation. Findings consistent with inflammation may be medically managed, whereas findings related to chronic stricture or fibrosis usually end up with surgical intervention [7].

In our 21 known cases of CD, 9 patients showed acute exacerbation on top of chronic disease, 12 cases showed chronic changes with non-obstructing stenotic segments; 9 cases in the ileum, one in the duodenum and two in the jejunum.

8 cases showed acute changes and presented for the first time with acute abdominal pain and diarrhea. One case was missed by MRE and showed minute jejunum aphthous ulcers and erosions by CE.

Extra intestinal findings and complications could not be evaluated by endoscopy and were only diagnosed by MRE. Endoscopic imaging does not yield information on perienteric or extraenteric changes, penetrating or fistulizing disease.

Fistula formation is common in CD, affecting between 17% and 50% of patients [28].

From our 30 cases, we found 3 perianal fistulas, 2 anterior wall fistulae and 2 enteroenteric fistulae, 2 enterovesical fistulae and 1 enterocolic fistula. The exact site and location of perianal fistulae were clearly seen on MRI, apart from one perianal fistula which was missed by MRE but clinically suspected and diagnosed on examination under anesthesia. We found that a dedicated high-resolution perianal MR protocol study is much more superior in detection of the minute subtle tracts.

Abscess is a frequent complication in CD, occurring in 10–30% of patients over the course of the disease [29]. The clinical challenge is twofold. First, the clinical and laboratory signs of abscess are often masked by immunosuppressant drugs taken. Second, abscess is a direct contraindication to biologic agents (including anti-TNFs) and corticosteroids [29].

Two of our cases showed deep intra-abdominal abscesses. MRE allowed detailed evaluation and proper location of the intra-

abdominal abscesses. Surgical intervention was immediately done and correlated well with our imaging findings.

Limitations in our study included insufficient small intestinal bowel distention in some cases and MRE missed small lesions and early ulcerations as compared to endoscopy.

In our study, MRE had a positive diagnostic impact in patients under investigation for CD and in those under follow-up, assisting gastroenterologists with their therapeutic strategy whether surgical or medical treatment.

5. Conclusion

Despite endoscopy remains the gold standard in diagnosis of Crohn's disease, MRE has shown to possess excellent sensitivity and specificity with comparable results to both CE and ileo-colonoscopy. MRE represents an ideal well-tolerated non-invasive imaging modality for initial evaluation, follow-up and assessment of therapeutic response, with the superior advantage of evaluation of extra-enteric complications of CD.

Conflict of interest

There is no conflict of interest.

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